Remarks

Reconsideration of this Application is respectfully requested.

Upon entry of the foregoing amendment, claims 41, and 52-62 are pending in the application, with claim 41 being the independent claim. Claims 42-51 have been cancelled without prejudice to or disclaimer of the subject matter therein.

Based on the above amendment and the following remarks, Applicants respectfully request that the Examiner reconsider all outstanding objections and rejections and that they be withdrawn.

Rejection under 35 U.S.C. § 112, first paragraph, Written Description

Claims 52, 55, 57, 58, 61 and 62 are rejected under 35 U.S.C. § 112, first paragraph, as allegedly failing to comply with the written description requirement. (Office Action, page 2.)

The test for the written description requirement is whether one skilled in the art can reasonably conclude that the inventor has possession of the claimed invention in the specification as filed. *Vas-Cath Inc. v. Mahurkar*, 935 F.2d 1555, 1563, 19 U.S.P.Q.2d 1111, 1116 (Fed. Cir. 1991); MPEP § 2163.02. The Federal Circuit has re-emphasized the well-settled principle of law that "[t]he written description requirement does not require the applicant 'to describe exactly the subject matter claimed, [instead] the description must clearly allow persons of ordinary skill in the art to recognize that [they] invented what is claimed.'" *Union Oil of Cal. v. Atlantic Richfield Co.*, 208 F.3d 989, 54 U.S.P.Q.2d 1227 (Fed. Cir. 2000). Furthermore, an applicant is not required to explicitly describe the subject matter. *Unocal*, 208 F.3d at 1000; *see also* MPEP § 2163.02 ("The

subject matter of the claim need not be described literally (*i.e.*, using the same terms or *in haec verba* in order for the disclosure to satisfy the description requirement.").

The Examiner has alleged that there is no support in the specification as originally filed for the composition of claim 52 and that the specification does not disclose the "scope of claim 52 which encompasses other types of composition containing nonpharmaceutically acceptable carrier." (Office Action, page 3.) Applicants respectfully traverse the rejection.

Applicants note that the Federal Circuit stated in *Univ. of Calif. v. Eli Lilly & Co.*, 43 U.S.P.Q.2d 1398 (Fed. Cir. 1997), that:

> A description of a genus of cDNAs may be achieved by means of a recitation of [1] a representative number of cDNAs, defined by nucleotide sequence, falling within the scope of the genus or [2] of a recitation of structural features common to the members of the genus, which features constitute a substantial portion of the genus . . . We will not speculate in what other ways a broad genus of genetic material may be properly described . . .

Univ. of Cal., 43 U.S.P.Q.2d at 1406. Thus, the Federal Circuit has stated that the written description requirement for a claim directed to a genus of molecules may be satisfied by providing the sequences of a representative number of molecules which fall within the scope of the genus. *See id.*

In the present case, Applicants have described several types of useful carriers which are known in the art, *e.g.*, thyroglobulin, albumins such as human serum albumin, tetanus toxoid, polyamino acids such as poly L-lysine, poly L-glutamic acid, influenza, hepatitis B virus core protein and the like. (*See* Specification, page 43, lines 1-4.) Thus, Applicants have described a representative number of different carriers within the

general category of the genus "carrier." In view of the standard for written description described above, Applicants assert that they are in possession of the claimed invention and that "a composition comprising the peptide of claim 41 and a carrier" is clearly supported in the specification such that one of skill in the art would have reasonably concluded that the inventor, at the time the application was filed, had possession of the invention as recited in claim 52.

The Examiner has stated that "the cited passage of the specification refers to vaccines and carriers for vaccines that constitute pharmaceutical carriers. The specification does not disclose the scope of claim 52 which encompasses other types of compositions containing nonpharmaceutically acceptable carriers." (Office Action, page 3.) The Examiner then states that a "[p]atent's entitlement to earlier filing date extends only to that which is disclosed in prior application, and does not extend to subject matter which is not disclosed, but would be obvious over what is expressly disclosed. . . . " (*Id.*) As discussed above, Applicants point out that the subject matter of claim 52 has been disclosed as a representative number of carriers have been described in the specification. Indeed, the Examiner also notes that "the cited passage of the specification refers to . . . carriers . . . that constitute pharmaceutical carriers." The pharmaceutical carriers described in the specification are examples of carriers in general, and thus adequately support claim 52.

With regard to the issue raised by the Examiner regarding "nonpharmaceutically acceptable carriers," Applicants note, as an initial matter, that this is not recited or claimed, and that the specification describing examples of carriers is sufficient to describe "carrier" as recited in claim 52. Furthermore, it is unclear what the Examiner

means by the term "nonpharmaceutically acceptable carrier." For example, water or saline solution are sometimes considered nonpharmaceutically acceptable carriers (depending on the active ingredient and method of administration), but sometimes these may also be considered as "pharmaceutically acceptable" carriers. Considering water or saline solution as examples of nonpharmaceutically acceptable carriers, Applicants assert that these types of carriers were well known to one of ordinary skill in the art at the time of the filing of the present invention.

The Examiner's citations to *Lockwood v. American Airlines Inc.* and *Eiselstein v. Frank* noting that "[a] description which renders obvious the invention for which an earlier filing date is sought is not sufficient" is misplaced. As discussed above, the specification contains adequate description supporting the term "carrier" in claim 52, and even assuming that there is a requirement that the specification also support the term "nonpharmaceutically acceptable carrier" (which there is not, and whose meaning has not been clarified by the Examiner), Applicants respectfully assert that water or saline solution, as examples of a hypothetical "nonpharmaceutically acceptable carrier," were well known to one of ordinary skill in the art at the time of filing of the invention. Accordingly, Applicants respectfully request that the rejection of claim 52 be reconsidered and withdrawn.

The Examiner has also alleged that there is no support in the specification for the recitation of "wherein said one or more second peptides is a cytotoxic T cell (CTL)-inducing peptide or a helper T cell (HTL)-inducing peptide" in claim 55. (Office Action, page 4.) Applicants respectfully disagree. Applicants note that the specification describes an epitope-based vaccine approach where "there is an ability to combine

selected epitopes (CTL and HTL) . . . ." (Specification, page 6, lines 27-28.) This description supports the concept that multiple peptide epitopes, CTL and/or HTL, can be combined into a single composition. In addition, the specification also notes that

> [A] polyepitopic peptide composition comprising multiple CTL and HTL epitopes that target greater than 98% of the population may be created for administration to individuals at risk for both HBV and HIV infection. The composition can be provided as a single polypeptide that incorporates the multiple epitopes from the various diseases-associated sources, *or can be administered as a composition comprising one or more discrete epitopes.*

(Specification, page 84, lines 27-32) (emphasis added). Thus, the specification contemplates that a second epitope, as recited in claim 55, can be a discrete CTL or HTL epitope. Thus, a second epitope corresponding to either a CTL or HTL peptide is fully supported by the specification.

The Examiner has also alleged that "[t]here is no support in the specification as originally filed for the composition of claims 61, 62." (Office Action, page 4.) In particular, the Examiner alleges that the specification "discloses the peptide of claim 61/62 linked to a CTL epitope . . . but does not disclose the claimed composition which is not a vaccine and wherein the peptides are not linked." (*Id.*) Applicants point out, as discussed above, that while the specification does describe embodiments where the CTL and/or HTL peptides of the invention are linked, that the specification also contrasts compositions where the peptides are provided together as a single polypeptide with compositions that "can be administered as a composition comprising one or more discrete epitopes." (Specification, page 84, lines 27-32.) Thus, in contrast to the Examiner's allegation, the specification provides support for compositions where the

CTL and/or HTL peptides of the invention are both linked or unlinked. Additionally, the different pharmaceutical or vaccine compositions described in the specification are examples of compositions according to the invention. Thus, the description of the different types of compositions fully support a composition according to claim 61 or 62.

The Examiner has further rejected claim 61 under 35 U.S.C. § 112, first paragraph, as allegedly failing to comply with the written description requirement because the "claims encompass a vast collection of artificial peptides with the functional attributes of a pan-DR binding epitope wherein the identity of said peptides is not disclosed in the specification and it appears unpredictable as to what peptides would or would have said functional attributes." (Office Action, pages 4 and 5.) Contrary to the Examiner's assertion, Applicants point out that the specification describes pan-DR binding epitopes:

> In certain embodiments, the T helper peptide is one that is recognized by T helper cells present in the majority of the populations. This can be accomplished by selecting amino acid sequences that bind to many, most, or all of the HLA class II molecules. These are known as "loosely HLA-restricted" or "promiscuous" T helper sequences. Examples of amino acid sequences that are promiscuous include sequences from antigens such as tetanus toxoid at positions 830-843 (QYIKANSKFIGITE), *Plasmodium falciparum* CS protein at positions 378-398 (DIEKKIAKMEKASSVFNVVNS), and Streptococcus 18kD protein at positions 116 (GAVDSILGGVATYGAA). Other examples include peptides bearing a DR 1-4-7 supermotif, or either of the DR3 motifs.

(Specification, page 50, line 28 to page 51, line 2.) Thus, the specification not only describes the functional attributes of a pan-DR binding epitope, but also provides several examples of well-known and frequently-utilized pan-DR binding epitopes. In view of

the above, one of ordinary skill in the art would readily and predictably understand what is meant by the term "pan-DR binding epitope."

In view of the discussion above, Applicants therefore assert that claims 52, 55, 57, 58, 61 and 62 satisfy the written description requirement of 35 U.S.C. § 112, first paragraph. Accordingly, Applicants respectfully assert that the Examiner withdraw the rejection.

Rejection under 35 U.S.C. § 112, first paragraph, Enablement

Claims 53 and 58 are rejected under 35 U.S.C. § 112, first paragraph, as allegedly failing to comply with the enablement requirement. (Office Action, page 6.)

Specifically, the Examiner reasserts the same statement as set forth in the previous substantive Office Action that "the specification does not disclose how to use the instant invention for the in vivo treatment/prevention of HBV in humans." (*Id.*) Applicants disagree and respectfully traverse the rejection.

In order for a claim to be enabled, the specification must teach one of ordinary skill in the art to make and use the invention without undue experimentation. The factors that can be considered in determining whether an amount of experimentation is undue have been set forth in *In re Wands*, 858 F.2d731, 737, 8 U.S.P.Q.2d 1400, 1404 (Fed. Cir. 1988). Among these factors are: 1) the guidance provided by the specification; 2) the amount of pertinent literature; 3) the presence of working examples; and 4) the predictability of the art. The test for undue experimentation is not merely quantitative, since a considerable amount of experimentation is permissible, if it is merely routine. *See id.*

As Applicants have noted previously, the Examiner's rejection is one based on "how to use." Applicants again remind the Examiner that

> [W]hen a compound or composition claim is not limited by a recited use, any enabled use that would reasonably correlate with the entire score of that claim is sufficient to preclude a rejection for nonenablement based on how to use . . . if any use is enabled when multiple uses are disclosed, the application is enabling for the claimed invention.

M.P.E.P. § 2164.01(c).

The Examiner's response to Applicants arguments is simply to state that the "the claimed invention is drawn to a pharmaceutical composition wherein the intended use for said composition disclosed in the specification is the in vivo treatment of disease in humans." (Office Action, page 8.) However, the Examiner's comments do not address Applicants argument that there is *no use limitation recited in the claims*. Applicants again assert that the instant claims are not limited by a recited use, so any enabled use disclosed in the specification enables the claims if the use is in keeping with their scope.

"As concerns the breadth of a claim relevant to enablement, the only relevant concern should be whether the scope of enablement provided to one skilled in the art by the disclosure is commensurate with the scope of protection sought by the claims." MPEP § 2164.08 (2006) (citing *AK Steel Corp. v. Sollac*, 344 F.3d 1234, 1244 (Fed. Cir. 2003); *In re Moore*, 439 F.2d 1232, 1236 (C.C.P.A. 1971); s*ee also Plant Genetic Sys., N.V. v. DeKalb Genetics Corp.*, 315 F.3d 1335, 1339 (Fed. Cir. 2003).

Without disclaiming or disparaging any of the uses disclosed by the specification, Applicants note that the enablement requirement does not require data showing treatment efficacy or any clinical use as it would appear that the Examiner would require.

Applicants assert that the "pharmaceutical composition" of claims 53 and 58 is simply one which contains the claimed peptides as well as, for example, pharmaceutically-acceptable excipients. This composition can be used, for example, to assay the activity of peptides in transgenic mice as described in Example 8 of the specification. Thus, Applicants have enabled the claimed invention for at least one use which correlates with the claimed invention.

"[A] specification disclosure which contains a teaching of the manner and process of making and using the invention . . . . must be taken as in compliance with the enabling requirement of the first paragraph of § 112 unless there is reason to doubt the objective truth of the statements contained therein which must be relied upon for enabling support." *Rasmusson v. Smithkline Beecham Corp.*, 413 F.3d 1318, 1323 (Fed. Cir. 2005) (quoting *In re Marzocchi*, 439 F.2d 220, 223 (C.C.P.A. 1971)). As discussed above, the application as filed provides an enabling disclosure of the presently claimed composition.

In addition, the Examiner appears to suggest that for the claimed invention to be enabled, Applicants must demonstrate the clinical efficacy of the claimed composition. Applicants wish to remind the Examiner, however, that there is no requirement for clinical data to prove that an application is in compliance with 35 U.S.C. § 112, first paragraph. In fact, description of *in vitro* and/or animal testing has been held to enable claims to *in vivo* therapeutic compositions and methods of their use. To this end, the Federal Circuit has stated that:

> In vitro testing, in general, is relatively less complex, less time consuming, and less expensive than in vivo testing. Moreover, in vitro results with respect to the particular pharmacological activity are generally predictive of in vivo

> test results, i.e., there is a reasonable correlation therebetween. Were this not so, the testing procedures of the pharmaceutical industry would not be as they are.

Cross v. Iizuka, 753 F.2d 1040, 1050 (Fed. Cir. 1985); *see also In re Brana*, 51 F.3d 1560, 1567-68 (Fed. Cir. 1995) (holding that animal testing results are sufficient to establish whether one skilled in the art would believe that a pharmaceutical compound has an asserted clinical utility for the purposes of compliance with the enablement requirement of 35 U.S.C. § 112, first paragraph). Thus, even assuming that Applicants would have to enable an artificially created use limitation recited in the claims, Applicants note that the specification provides *in vitro*, as well as *in vivo* assays, as to how the peptides and compositions of the invention would be assayed, for example, for their immunogenicity using animals.

In view of the forgoing discussion, Applicants submit that a person having ordinary skill in the art, in view of the teachings of the specification and the knowledge in the art, would be able to make and practice the full scope of Applicants' claimed invention. In addition, Applicants contend that the Examiner has failed to provide an acceptable legal basis for requiring Applicants to enable a use limitation that is not even recited in the claims. Accordingly, Applicants respectfully request that this rejection of the claims under 35 U.S.C. § 112, first paragraph, be reconsidered and withdrawn.

Rejection of Claim 41/43

The Examiner has stated "claim 41/43 is interpreted as encompassing the peptide recited in the claim attached to another peptide(s)." (Office Action, page 9.) Applicants assert that the Examiner appears to be reintrepreting the recited claim without providing

any discernible reasoning. Applicants note that claim 41 is directed to "[a]n isolated peptide less than 15 amino acids in length comprising an oligopeptide selected from the group consisting of: QAFTFSPTYK (SEQ ID NO:638); LVVDFSQFSR (SEQ ID NO:620); NVSIPWTHK (SEQ ID NO:625); and SAICSVVRR (SEQ ID NO:653)."

The Examiner has appeared to attach his own meaning to the words of the claim by alleging that "applicant intended that claim 41 encompass the peptide of claim 41 attached to other peptides and wherein the aggregate length of the peptide complex is greater than the 15 amino acids of the isolated peptide portion of the peptide complex." (Office Action, page 10.) The Examiner has provided no basis for this created meaning. Claim 41 clearly states that the claimed peptide is less than 15 amino acids in length. Thus, it is difficult to understand how the Examiner is interpreting the "aggregate length of the peptide complex" as "greater than 15 amino acids." Without acquiescing to the Examiner's rejection, Applicants note that claim 43 has been cancelled. Applicants respectfully assert that the meaning of claim 41 is clear, and request that the Examiner withdraw this rejection.

Rejection under 35 U.S.C. § 102

Claims 41, 43, 46, 52, 53, 55, 57, and 58 are rejected under 35 U.S.C. § 102(e) as allegedly being anticipated by Seeger *et al.* (Seeger), U.S. Patent No. 5,360,714, as evidenced by Pasek *et al.* (Pasek). (Office Action, page 10.) Applicants respectfully disagree and traverse the rejection.

A claim is anticipated only if each and every element as set forth in the claim is found, either expressly or inherently described, in a single prior art reference. *Verdegaal*

Bros. v. Union Oil Co. of California, 814 F.2d 628, 631 (Fed. Cir. 1987); MPEP § 2131. Seeger fails to teach every aspect of the claimed invention.

Without acquiescing to the Examiner's rejection, Applicants note that claims 43 and 46 have been cancelled. Independent claim 41 is directed to an isolated peptide *less than 15 amino acids in length*. Seeger does not disclose the exact peptide as recited in claim 41. Seeger only discloses a peptide sequence that *comprises* Applicants' claimed peptide. (*See* Seeger, col. 10, 3rd paragraph, col. 5, 3rd paragraph, cols 11-12.)

With respect to dependent claims 52, 53, 55, 57, and 58, Applicants note that "[t]he standard for lack of novelty under 35 U.S.C. §102, that is, for 'anticipation,' is one of strict identity." *See* Chisum, Donald S., *Chisum on Patents*, 1:3.02[1], Matthew Bender & Co., Inc. (2002). To anticipate a claim, a single source of prior art must disclose all of the limitations (sometimes called elements) of the claim. *See id.* As stated by the Federal Circuit in *PPG Indus., Inc. v. Guardian Indus. Corp.*, 75 F.3d 1558, 1566 (Fed. Cir. 1996): "[t]o anticipate a claim, a reference must disclose every element of the challenged claim and enable one skilled in the art to make the anticipating subject matter." The absence of any claimed element from the reference negates anticipation. *Minn. Mining & Mfg.*, 976 F.2d at 1572 (*citing Atlas Powder Co. v. E.I. du Pont de Nemours & Co.*, 750 F.2d 1569, 1574 (Fed. Cir. 1984)).

Dependent claims 52, 53, 55, 57, and 58 depend, either directly or indirectly, from claim 41, and therefore incorporate all of the limitations of claim 41. *See* 35 U.S.C. § 112, fourth paragraph. As discussed above, Seeger does not does not disclose the exact peptide as recited in the claim 41. Dependent claims 52, 53, 55, 57, and 58

incorporate the limitations of claim 41, and therefore, Seeger also does not disclose all of the limitations of claims 52, 53, 55, 57, and 58.

As to § 102 anticipation rejections, if an independent claim is not fully met by an alleged prior art reference, neither are the more limited dependent claims. *See Application of Royka,* 490 F.2d 981, 983-984 (Cust. & Pat. App. 1974). "It is elementary that to support an anticipation rejection, all elements of the claim must be found in the reference." Indeed, in *Royka*, the Board found that "[t]he dependent claims rejected with [independent] claim 28, as anticipated under § 102, are not anticipated since [independent] claim 28 is not anticipated." *Id.*

Seeger does not disclose the peptide recited in claim 41, nor does it additionally disclose the further limitations of claims 52, 53, 55, 57, and 58.

Thus, for at least the reasons discussed above, Applicants assert that Seeger does not teach all of the limitations of claims 41, 52, 53, 55, 57, and 58. Consequently, Seeger does not anticipate these claims. As such, Applicants respectfully request that the rejection of these claims under 35 U.S.C. § 102(e) be reconsidered and withdrawn.

Conclusion

All of the stated grounds of objection and rejection have been properly traversed, accommodated, or rendered moot. Applicants therefore respectfully request that the Examiner reconsider all presently outstanding objections and rejections and that they be withdrawn. Applicants believe that a full and complete reply has been made to the outstanding Office Action and, as such, the present application is in condition for allowance. If the Examiner believes, for any reason, that personal communication will expedite prosecution of this application, the Examiner is invited to telephone the undersigned at the number provided.

Prompt and favorable consideration of this Amendment and Reply is respectfully requested.

Respectfully submitted,

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